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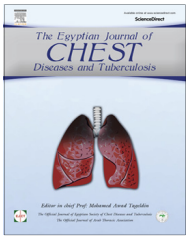

ORIGINAL ARTICLE

Correlation of respiratory pump function with symptomatology in COPD

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KEYWORDS

Respiratory muscle function;
COPD;
Respiratory center drive

Abstract Staging criteria for COPD include symptoms and lung function parameters, but the role of respiratory pump function parameters in determining disease severity remains unclear.

This study aimed to assess the correlation of respiratory pump functions including respiratory center drive (P0.1), inspiratory muscle strength (PImax) and respiratory muscle fatigue (P0.1/P0.1max%) and symptomatology in COPD patients.

This study was carried out on 80 COPD patients recruited from the outpatient clinic of Chest Department, Tanta Faculty of Medicine. They had obstructive airflow limitation with FEV1/FVC% <70% and their reversibility tests were lower than 12%. All patients were classified according to GOLD 2015 into 4 grades (A–D).

Respiratory center drive (P0.1), respiratory muscle strength (PImax), respiratory muscle fatigue (P0.1/P0.1max%) were assessed in all patients and correlated to COPD symptomatology.

The results of this study showed that P0.1 and P0.1/P0.1max% were significantly higher in grade B&D compared to grade A&C ($p < 0.01$) and significantly higher in grade D compared to grade B ($p < 0.05$), while PImax was significantly lower in grade B&D compared to grade A&C ($p < 0.01$) and significantly higher in grade D compared to grade B ($p < 0.05$).

P0.1, PImax and P0.1/P0.1max% and resting arterial carbon dioxide tension showed a significant positive correlation with disease symptomatology (CAT and mMRC scales) in COPD patients ($p < 0.05$) while there was an insignificant correlation between FEV1% of predicted and disease symptoms in the studied patients.

It was concluded that, respiratory pump functions as reliably assessed by P0.1. PImax and P0.1/P0.1max% can be considered as an important factor in rating disease severity and correlate significantly with symptomatology in COPD patients.

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic disease characterized by the loss of lung elasticity and airway narrowing resulting in airflow limitation [1]. This progressive

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airflow limitation leads to chronic air trapping and hyperinflation, especially during activity or exercise. Hyperinflation causes mechanical disadvantages since it depresses the diaphragm and impairs intercostal muscle contractility. This impairment increases the work and metabolic expenditure associated with breathing and contributes to breathlessness [2].

In the diagnosis of COPD, spirometry has been used as an objective measure to confirm its symptom-based clinical suspicion. The diagnostic criteria for COPD include a forced expiratory volume in one second/forced vital capacity ratio (FEV1/FVC) less than 70% of predicted value. FEV1 in patients with COPD is used to grade the severity of airway obstruction and as the main predictor of both disease progression and mortality [3].

Patients with COPD often exhibit respiratory muscle weakness and reduced respiratory muscle endurance. Respiratory muscles are submitted to multiple factors related to both the presence and severity of COPD which may impair their structure and function [4].

The imbalance between the respiratory muscle strength and the load, they are chronically facing, plays an important role in the genesis of dyspnoea and hypercapnia. It has also been described that respiratory muscle dysfunction could be an important determinant of increased use of health resources and survival in hospitalized patients with severe COPD [5].

Inspiratory mouth occlusion pressure at 100 ms during quiet breathing (P0.1) is a marker of neuromuscular ventilatory drive which is independent of the patient's effort. P0.1 and the ratio of P0.1/PImax have been suggested as predictors of impending respiratory muscle fatigue. Therefore, it may be hypothesized that these measures also play a role for long-term outcome in patients with COPD [6].

Patients and methods

This study was carried on 80 COPD patients recruited from the outpatient clinic of Chest Department, Tanta Faculty of Medicine. They had obstructive airflow limitation with FEV1/FVC% $<70\%$ and their reversibility tests were lower than 12%. All the patients were clinically stable and had been receiving optimal medical therapy according to their group classification.

All the patients signed the written informed consent approved by the ethics committee.

Patients were excluded from the study if they had:

- Past or family history suggesting asthma.
- Reversibility test higher than 12%.
- Active heart disease.
- Neuromuscular diseases.
- Disabling diseases that interfere with the tests.

All patients were classified according to GOLD 2015 [7] criteria in 4 equal grades according to airflow limitation, Symptoms & breathlessness, exacerbation history and previous hospital admission.

The following was done for all patients:

- Post broncho-dilatation spirometric data including FVC% of predicted, FEV1% of predicted and FEV1%.
- Functional dyspnea was assessed using:
  - Modified Medical Research Council Scale (mMRC) which include 5 grades of physical activities that provoke dyspnea and ranged from 0 (non exertional dyspnea at all) to 4 (Breathlessness on dressing or undressing).
  - COPD Assessment Test (CAT) ranging from 0 to 40.
- Number of exacerbations and hospital admission in the last year.
- Respiratory pump function was done using ResPImax (Andos, Hamburg, Germany Apparatus) and includes the following:
  - *Respiratory center drive (P0.1):* Measures the mouth occlusion pressure after 0.1 s from initiation of inspiration. Patient was asked to breathe quietly in sitting position through the mouth piece of the apparatus fitting tightly inside the lips of the patient to prevent leakage. The test was repeated 6 times and the mean value was calculated.
  - *Respiratory muscle strength (PImax):* It was measured from residual volume at maximal inspiratory effort while recording peak inspiratory pressures. The test was repeated six times and the maximal value was recorded.
  - *Respiratory muscle fatigue:* It was assessed by calculating P0.1/P0.1max%
- *Arterial blood gases:* $PaCO_2$ was measured at rest while breathing room air using blood gas analyzer.

Results

This study was carried out on 80 COPD patients attending the outpatient clinic of the Chest Department, Tanta Faculty of Medicine. All of them were males. They were classified into 4 equal groups according to GOLD severity grading (A–D) criteria.

All the patients were statistically matched as regards age, body mass index BMI and smoking index (Table 1).

Respiratory center drive (P0.1)

One way analysis of variance in the four studied COPD grades showed statistically significant difference, ($F = 14.32$, $p < 0.05$). Pairwise multiple comparisons (Tukey test) showed that P0.1 was significantly higher in grade B&D compared to grade A&C ($p < 0.01$) and significantly higher in grade D compared to grade B ($p < 0.05$).

Respiratory muscle strength (PImax)

One way analysis of variance in the four studied COPD grades showed statistically significant difference, ($F = 8.81$, $p < 0.05$). Pairwise multiple comparisons (Tukey test) showed

Table 1 Patient characteristics in the four studied groups.

	Age (years)	Body mass index BMI (kg/m^2)	Smoking index (pack/year)
Grade A	59.2 ± 2.3	26.2 ± 1.5	45 ± 22
Grade B	63.1 ± 1.9	25.9 ± 1.2	43 ± 20
Grade C	61.7 ± 2	25.5 ± 1.6	46 ± 23
Grade D	62.5 ± 1.8	26 ± 1.7	45 ± 21

that PImax was significantly lower in grade B&D compared to grade A&C ($p < 0.01$) and significantly lower in grade D compared to grade B ($p < 0.05$).

Respiratory muscle fatigue (P0.1/P0.1max%)

One way analysis of variance in the four studied COPD grades showed statistically significant difference, ($F = 11.12$, $p < 0.05$). Pairwise multiple comparisons (Tukey test) showed that P0.1/P0.1max% was significantly higher in grade B&D compared to grade A&C ($p < 0.01$) and significantly higher in grade D compared to grade B ($p < 0.05$) (Table 2).

Arterial carbon dioxide tension ($PaCO_2$) (Fig. 1)

One way analysis of variance in the four studied COPD grades showed statistically significant difference, ($F = 10.15$, $p < 0.05$). Pairwise multiple comparisons (Tukey test) showed that $PaCO_2$ mmHg was significantly higher in grade B&D compared to grade A&C ($p < 0.01$) and significantly higher in grade D compared to grade B ($p < 0.05$).

Correlation between FEV1% of predicted and COPD symptomatology

In this study, there was an insignificant correlation between FEV1% of predicted and COPD symptomatology CAT and mMRC ($r = 0.572$ and 0.541 respectively, $p > 0.05$) (Figs. 2 and 3).

In this study, there were significant positive correlations between respiratory center drive function (P0.1) and COPD symptomatology CAT and mMRC ($r = 0.94$ and 0.875 respectively, $p < 0.05$) (Figs. 4 and 5).

In this study, there were significant negative correlations between inspiratory muscle strength function (PImax) and

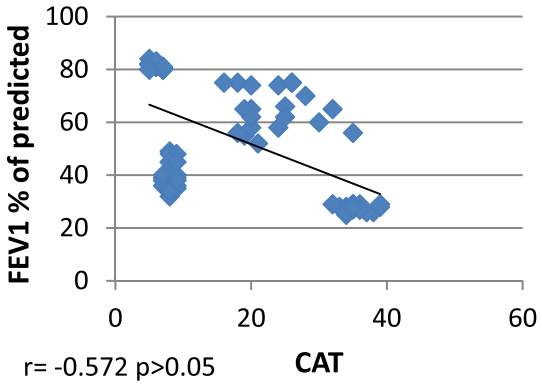

Figure 2 Correlation between CAT and FEV1% of predicted in COPD patients.

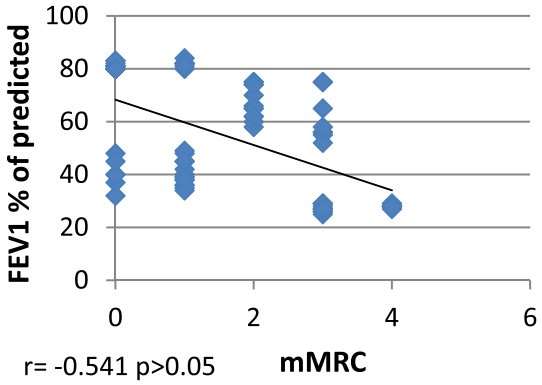

Figure 3 Correlation between mMRC and FEV1% of predicted in COPD patients.

Table 2 Patients classification according to GOLD grading criteria.

	FVC% of predicted	FEV1% of predicted	FEV1%	mMRC scale	CAT scale	No. of exacerbations	No. of hospital admissions
Grade A	81.35 ± 1.04	81.25 ± 1.21	68.65 ± 0.75	0.35 ± 0.49	5.9 ± 0.85	0.45 ± 0.51	0
Grade B	66 ± 7.02	64.9 ± 7.81	63.8 ± 3.35	2.4 ± .05	23.3 ± 5.11	0.65 ± 0.49	0
Grade C	42.15 ± 4.53	40.3 ± 4.93	52.05 ± 4.11	0.7 ± 0.47	8.2 ± 0.77	2.55 ± 0.69	1.45 ± 1.51
Grade D	27.85 ± 0.93	27.6 ± 1.19	41.7 ± 2.99	3.45 ± 0.51	35.5 ± 1.82	4.35 ± 0.93	3.7 ± 0.73

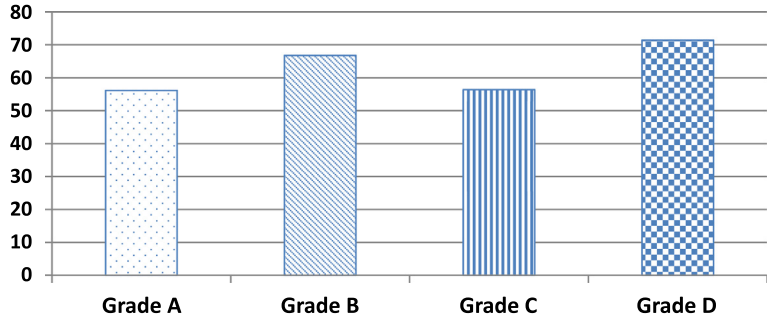

Figure 1 Resting arterial carbon dioxide tension (mmHg) in the 4 COPD grades.

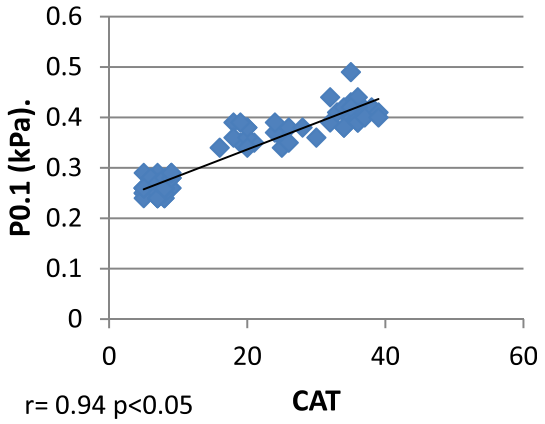

Figure 4 Correlation between CAT and P0.1 in COPD patients.

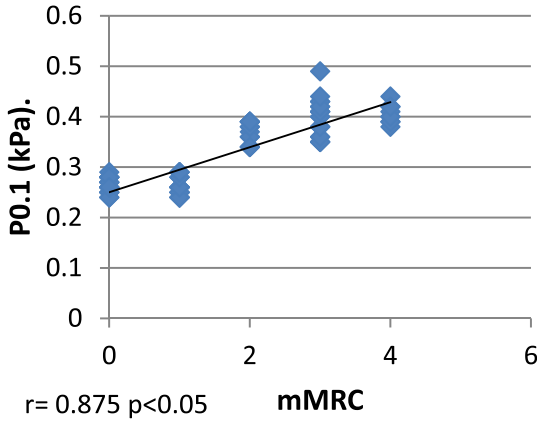

Figure 5 Correlation between mMRC and P0.1 in COPD patients.

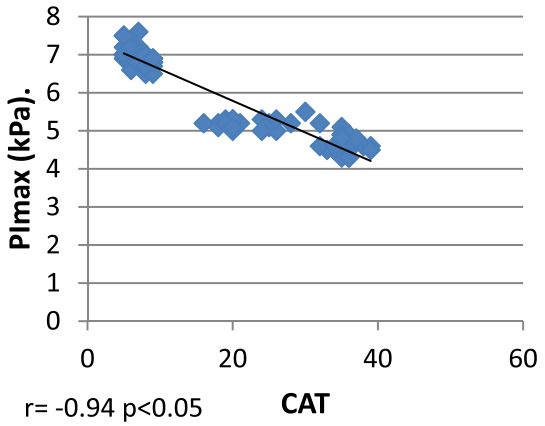

Figure 6 Correlation between CAT and PImax in COPD patients.

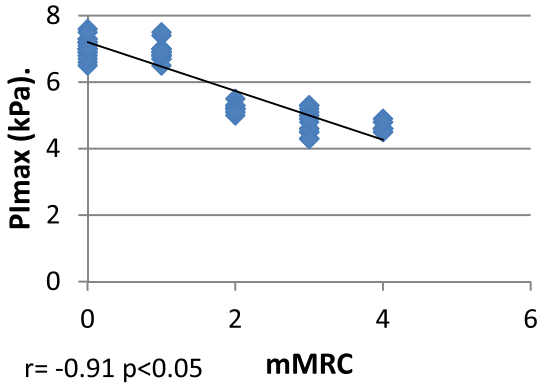

Figure 7 Correlation between mMRC and PImax in COPD patients.

COPD symptomatology CAT and mMRC ($r = -0.94$ and -0.91 respectively, $p < 0.05$) (Figs. 6 and 7).

In this study, there were significant positive correlations between respiratory muscle fatigue function (P0.1/P0.1max%) and COPD symptomatology CAT and mMRC ($r = 0.95$ and -0.9 respectively, $p < 0.05$) (Figs. 8 and 9).

In this study, there were significant positive correlations between arterial carbon dioxide tension ($PaCO_2$ mmHg) and COPD symptomatology CAT and mMRC ($r = 0.94$ and 0.87 respectively, $p < 0.05$) (Figs. 10 and 11).

Discussion

Dyspnea is one of the leading symptoms affecting patients suffering from COPD. Development of dyspnea in patients of COPD is multifactorial and has been shown to be related to the degree of airway obstruction, pulmonary gas exchange abnormalities, inspiratory muscle strength, lung hyperinflations, respiratory central outputs and nutritional status [8] (Table 3).

In this study, all the patients were matched as regards age, sex and body mass index. It had been found that the degree of airway obstruction measured by the FEV1 was insignificantly

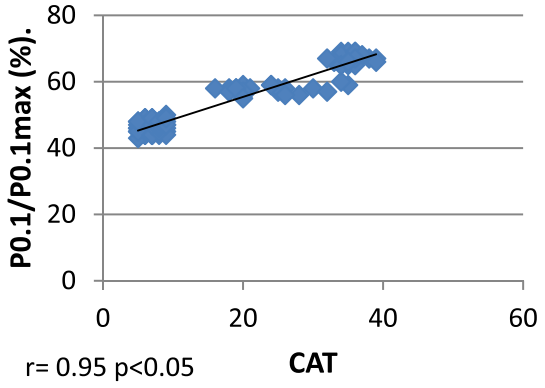

Figure 8 Correlation between CAT and P0.1/P0.1max in COPD patients.

correlated with the CAT and mMRC score respectively. This was consistent with a study which demonstrated that FEV1 has a poor correlation with clinical definition with COPD and suggested that inspiratory capacity (IC) could correlate better than FEV1 with dyspnea score and quality of life [9].

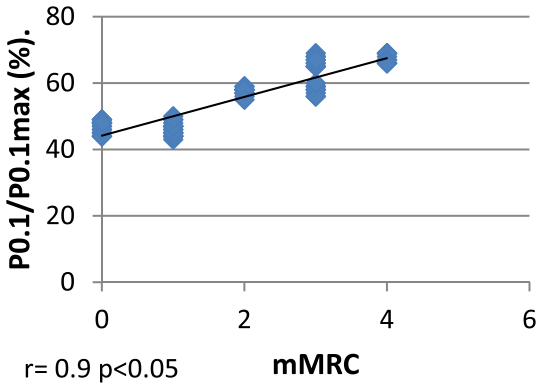

Figure 9 Correlation between mMRC and P0.1/P0.1max in COPD patients.

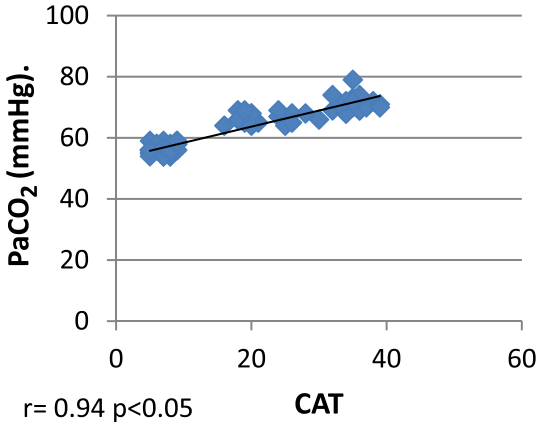

Figure 10 Correlation between CAT and $PaCO_2$ in COPD patients.

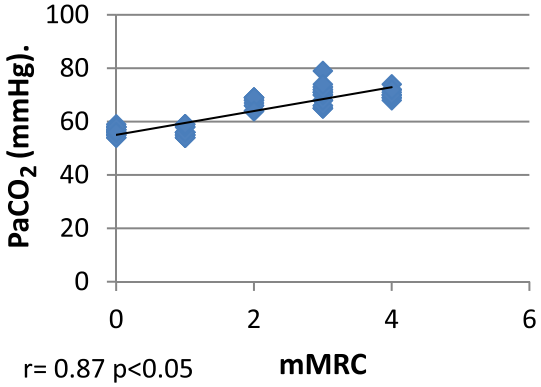

Figure 11 Correlation between mMRC and $PaCO_2$ in COPD patients.

FEV1 has a limited application in clinically assessing COPD patients. For example, patients with mild diseases (FEV1 higher than 80% of predicted value) or even patients with severe or very severe diseases (less than 50% of the predicted value) show a poor correlation between FEV1 and their clinical situation [10].

Table 3 Respiratory pump function in the 4 studied group grading.

	P0.1 (kPa)	PImax (kPa)	P0.1/P0.1max (%)
Grade A	0.26 ± 0.02	7.15 ± 0.24	45.85 ± 1.9
Grade B	0.37 ± 0.02[a]	5.19 ± .13[a]	57.55 ± 1.15[a]
Grade C	0.26 ± 0.02	6.81 ± .14	46.85 ± 1.79
Grade D	0.41 ± 0.3[a,b]	4.61 ± 0.19[a,b]	66.65 ± 2.08[a,b]

kPa: kilo pascal.
[a] Significant compared to grade A&C.
[b] Significant compared to grade B.

Clinical experience demonstrated that patients sharing similar FEV1 values could show different clinical parameters as regards degree of dyspnea and show marked difference in quality of life [11]. In COPD, hyperinflation or air trapping is the result of airway obstruction and destruction of the lung parenchyma and its vasculature. In recent years, the dynamic hyperinflation in these patients has been recognized as a factor that results in progression of dyspnea [12].

This study showed increased baseline P0.1 in all COPD patients. This can be explained by high neural drive to inspiratory muscle due to increased airflow resistance, abnormal blood gas exchange, weak respiratory muscle and high ventilatory requirements [13].

In this study, P0.1, PIMax and P0.1/P0.1max% showed significant correlation in all COPD patients with mMRC and CAT score.

Respiratory muscles are submitted to multiple factors related to both the presence and severity of COPD which may impair their structure and function such as changes in the chest wall geometry and diaphragm position, deleterious shortening of the diaphragm sarcomere length, activation of protease inspiratory muscles, oxidative stress, resting $PaCO_2$ which were significantly correlated with CAT and mMRC scores [5].

A study tested whether inspiratory muscle strength is reduced in COPD and is related to disease severity according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria and assessed its clinical impact. PImax (maximal inspiratory mouth occlusion pressure), SnPna (sniff nasal pressure) and TwPmo (twitch mouth pressure) following bilateral anterior magnetic phrenic nerve stimulation were assessed in 33 COPD patients (8 GOLD(0), 6 GOLD(I), 6 GOLD(II), 7 GOLD(III) and 6 GOLD(IV)) and in 28 matched controls. Furthermore, all participants performed a standardized 6 min walking test. In comparison with controls, PImax (11.6 ± 2.5 compared with 7.3 ± 3.0 kPa; $p < 0.001$), SnPna (9.7 ± 2.5 compared with 6.9 ± 3.3 kPa; $p < 0.001$) and TwPmo (1.6 ± 0.6 compared with 0.8 ± 0.4 kPa; $p < 0.001$) were markedly lower in COPD patients. TwPmo decreased with increasing COPD stage. TwPmo was correlated with walking distance ($r = 0.75$; $p < 0.001$), dyspnoea ($r = -0.61$; $p < 0.001$) and blood gas values following exercise ($r > 0.57$; $p < 0.001$). Inspiratory muscle strength, as reliably assessed by TwPmo, decreased with increasing severity of COPD and should be considered as an important factor in rating disease severity and to reflect burden in COPD [14].

In this study, hypercapnia correlated significantly with symptomatology in all COPD patients.

Chronic hypercapnic respiratory failure pathophysiologically, results from disturbances in the respiratory pump by mechanical disadvantage, central nervous system abnormalities or respiratory muscle dysfunction. Chronic hypercapnia is commonly considered an ominous prognostic sign, but the corresponding hypoventilation could also be favorable in preventing respiratory muscle fatigue [15].

Conflict of interest

The author declare that there is no conflict of interest.

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